

Numbers described herein in view of Matthews and Kricka, *Analytical Biochemistry* 169:1-25, 1988, referred to herein as "Matthews". Claims 1, 6-19, 45-46 and 58-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in such a way as to convey to one of skill in the art that the inventors were in possession of the claimed invention at the time the application was filed. Claims 1, 6-19, 23, and 45-63 were variously rejected under the judicially created doctrine of obviousness type double patenting over claims 1-9 of U.S. Patent No. 5,892,010 or non-elected claims 1-21, and 25-29 in co-pending USSN 08/785,532. Applicants respectfully traverse these rejections.

35 U.S.C. §112, second paragraph.

Claims 8, 9, 18 and 60-62 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. In particular, the Examiner objected to the recitation "hybridizes under stringent conditions" or "hybridizes" in claims 8, 60, and 61 without specifying stringency conditions. The Examiner further objected to the recitation of "the nucleic acid of 45" in Claim 18 as allegedly indefinite for failing to clarify the claim dependency. Applicants respectfully traverse by amendment and argument.

Claims 8, 60, and 61 are amended herein to recite "hybridizes under said stringent conditions" thereby obviating the Examiner's rejection. Furthermore, Applicants have expressly defined "said stringent conditions" at least in claim 1 and in the specification at least on page 6, lines 17-20 thus rendering claims 8, 60, and 61 clear and definite. Applicants respectfully request that the 112, second paragraph rejection of these claims be withdrawn.

No reason was given for the rejection of claims 9 and 62 for indefiniteness. Because claims 9 and 62 depend from definite claims 8 and 61 respectively and the Examiner has not indicated any other basis for the indefiniteness rejection of these claims, withdrawal of the 112, second paragraph rejection is respectfully requested.

Claim 18 is amended herein to recite "the nucleic acid of claim 45" thus clarifying the dependency of the claim. Applicants respectfully request that the 112, second paragraph rejection of this claim be withdrawn.

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35 U.S.C. §103(a).

Claims 1, 6, 8, 10, 12, 14, 16, 18, 23, and 45-46 were variously rejected under 35 U.S.C. §103(a) as allegedly obvious over various Accession Numbers as summarized below in **Table 1**, taken with Matthews and Kricka, *Analytical Biochemistry* 169:1-25, 1988.

Table 1. Summary of specific rejections correlating Accession Numbers with SEQ ID NOs.

Item	GenBank Accession No	SEQ ID NO
Item 9:	N32481, N93893, or G11697	(SEQ ID NO. 4);
Item 11:	H16953, 16954 or H12950	(SEQ ID NO. 5);
Item 13:	H40682	(SEQ ID NO. 6);
Item 15:	G27410, or G25553	(SEQ ID NO. 7);
Item 17:	N78571	(SEQ ID NO. 8);
Item 19:	N70546	(SEQ ID NO. 9);
Item 21	WO5407	(SEQ ID NO. 10);

In particular, the Examiner alleges that the cited Accession Numbers teach polynucleotide sequences that would hybridize to the indicated sequences under stringent conditions. The Examiner acknowledges that the cited Accession Numbers do not teach labeled sequences. The Examiner states that Matthews teaches methods for labeling polynucleotide sequences with various detectable labels for use as probes in a wide range of methods, such as restriction enzyme site mapping and RNA or DNA quantitation assays. The Examiner alleges that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to label the polynucleotide sequence taught by the Accession Number by the methods taught by Matthews for use as probes in the further characterization of the polynucleotide sequences taught by the Accession Numbers. Applicants respectfully traverse.

A) SEQ ID 9 and SEQ ID 10 (claims 1, 16, 18, 23, 45-46).

With respect to Items 19 and 21, SEQ ID NOs: 9 and 10, Applicants submit that Applicants invented the presently claimed invention before the publication date of these GenBank deposits. Upon an indication of otherwise allowable subject matter, Applicants will submit a declaration under 37 C.F.R. §1.131, swearing behind Accession Numbers N70546 and WO5407.

B) SEQ ID Nos: 4, 5, 6, 7, and 8 (Items 9, 11, 13, 15, and 17, claims 1, 6, 8, 10, 12, 14, 23, 45-46)

The Examiner is respectfully reminded that in order to find an invention *prima facie* obvious, the cited art must (1) teach or suggest each of the elements of the claimed invention, (2) provide suggestion or motivation to combine or modify the references, and (3) provide a reasonable expectation that one could successfully arrive at the claimed invention. See M.P.E.P. §2143 *et seq.* Applicants submit that the Examiner has failed to make her *prima facie* case because there is no suggestion or motivation to combine or modify the references cited.

The Examiner is reminded that an obviousness rejection requires a teaching or suggestion to modify the references in a manner indicated by the Examiner. As stated by the Court of Appeals for the Federal Circuit:

Our case law makes clear that the best defence against hindsight-based obviousness analysis is the rigorous application of the requirement for a showing of a teaching or motivation to combine the prior art references. See *Dembiczak*, 175 F.3d at 999, 50 USPQ2d at 1617. **“Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor’s disclosure as a blueprint for piecing together the prior art to defeat patentability--the essence of hindsight.”** *Id.* [emphasis added] *Ecolochem, Inc. v Southern-California Edison Co.*, 227 F.3d 1361, 1371 (Fed. Cir. 2000).

* * *

The mere fact that the prior art may be modified in the manner suggested by the Examiner **does not** make the modification obvious unless the prior art suggested the desirability of the modification. [emphasis added] *In re Fritch*, 23 USPQ 2d 1780, 1783-1784 (Fed. Cir. 1992).

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The presently pending claims incorporate a limitation which is not present in the cited Accession Numbers. Claim 1 recites in part:

“[a]n isolated nucleic acid molecule comprising a labeled polynucleotide sequence that hybridizes under stringent conditions to a sequence or the complement of a sequence selected from the group consisting of . . .” [emphasis added]

As recognized by the Examiner, the cited Accession Numbers do not teach labeled polynucleotide sequences. Moreover, GenBank offers no teaching or motivation that would lead one ordinary skill in the art to select the particular nucleic acids recited in pending claim 1 for labeling (i.e., for use as probes).

Lacking the specific teaching provided in the present specification there is nothing that would lead one of skill to select the particular ESTs identified by the Examiner from all the millions of sequences present in GenBank. The polynucleotide sequence contained in each Accession Number is an expressed sequence tag (“EST”), which has no defined function. The descriptive information published along with each cited EST also does not provide any information about the use or putative significance of the respective nucleotide sequence. Moreover, the Examiner has not articulated any teaching or suggestion in the prior art that would lead one of skill in the art to label the particular sequences disclosed in the cited accession numbers.

This defect of the GenBank sequence listings (accession numbers) is not remedied by Matthews. Matthews is a general review article and teaches various methods for labeling any DNA or RNA to generate polynucleotide probes. Matthews offers no teaching or suggestion regarding the particular ESTs identified by the Examiner. There is simply no teaching in Matthews that would lead one of skill to select and label the particular sequences identified by the Examiner rather than any of the millions of other sequence identified in GenBank.

Again, the Examiner is reminded that

[T]here still must be evidence that “a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed” *In re Rouffet*, 149 F.3d at 1357, 47 U.S.P.Q. 2D (BNA) at 1456; see also *In re Werner Kotzab*, 217 F.3d 1365, 1371, 55 U.S.P.Q. 2D (BNA) 1313, 1317 (Fed. Cir. 2000) (“A rejection cannot be predicated

on the mere identification . . . of individual components of claimed limitations. Rather, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.”) Here, there was no such evidence presented. *Ecolochem, Inc.* 227 F.3d. at 1375.

Stating that each of the cited Accession Numbers can be labeled and used as probes to further characterize the polynucleotide sequences taught by the Accession Numbers because each of the Accession Numbers hybridizes to their respective SEQ ID NO., as identified in Table 1, **does not constitute “particular findings”** as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected the components for combination in the manner claimed.

The Examiner is, at best, taking the present inventor’s own disclosure “as a blueprint for piecing together the prior art to defeat patentability--the essence of hindsight”. Without the teaching provided in the present specification, there is nothing that would lead one of skill in the art to produce the presently claimed labeled nucleic acids. The Examiner has failed to make a *prima facie* case of obviousness, and accordingly, the Applicants respectfully request that the §103 rejections made in Items 9, 11, 13, 15, and 17 be withdrawn.

35 U.S.C. §112, first paragraph.

Claims 1, 6-19, 45-46 and 58-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in such a way as to convey to one of skill in the art that the inventors were in possession of the claimed invention at the time the application was filed. Specifically, the Examiner states that the above identified claims are drawn to isolated nucleic acid molecules comprising a polynucleotide sequence that hybridizes under defined high stringency conditions to a sequence selected from the group consisting of SEQ ID No: 2-10 and 12. The Examiner also states that the claims are drawn to a large genus of polynucleotides that hybridize to SEQ ID No: 2-10 and 12, including each specific disclosed sequence and also polynucleotide sequences which embrace a wide range of substitutions, insertions, and deletions throughout the entire range of the reference SEQ ID NO., and the genes encoding these polynucleotide sequences. The Examiner further states that the specification demonstrates a reduction to practice of only a single species for each genus SEQ ID NO: 2-10 and 12, and the specification provides no disclosure of any elements of a gene or the characterization of any mutations. Finally, the Examiner states that all of

these elements must be described and the Examiner directs the Applicants to the Revised Interim Guidelines *Written Description Requirement, Federal Register, Vol: 64, No. 244, pages 71427-71440, Tuesday, December 21, 1999*. Applicants respectfully traverse this rejection.

The Examiner is reminded:

These revised interim "Written Description Guidelines" are intended to assist Office personnel in the examination of patent applications for compliance with the written description requirement of 35 U.S.C. §112, para. 1. . . .

This revision **does not constitute substantive rule making and hence does not have the force and effect of law**. It is designed to assist Office personnel in analyzing claimed subject matter for compliance with substantive law. Rejections will be based on the substantive law, and it is these rejections which are appealable. . . .

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. Possession may be shown by actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or other descriptions of the invention that are sufficiently specific to enable a person skilled in the art to practice the invention. [emphasis added] *Written Description Requirement, Fed. Reg., Vol: 64, No. 244, pages 71427-71440, Tuesday, December 21, 1999, page 71434*.

Recently, the Court of Appeals for the Federal Circuit ("CAFC") reiterated that "[i]n written description cases, 'the primary consideration is factual and depends on the nature of the invention and the amount of knowledge imparted to those of skill in the art by the disclosure.'" *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 996 (Fed. Cir. 2000), quoting *In re Wertheim*, 541 F.2d 257, 262 (CCPA 1976). The CAFC also stated:

The written description requirement does not require the applicant 'to describe exactly the subject matter to be claimed, instead the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.'" *Id.* at 997, quoting *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

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The CAFC further states:

Rather, the Patent Act and this court's case law require only sufficient description to show one of skill in the refining art that the inventor possessed the claimed invention at the time of filing."
Id.

Here, the Applicants claim "[a]n isolated nucleic acid molecule comprising a labeled polynucleotide sequence that hybridizes under stringent conditions to a sequence or to a complement of a sequence selected from a group consisting of SEQ ID No. 2, SEQ ID No. 3, SEQ ID No. 4, SEQ ID No. 5, SEQ ID No. 6, SEQ ID No. 7, SEQ ID No. 8, SEQ ID No. 9, and SEQ ID No. 10, wherein said stringent conditions comprise a 0.02 molar salt concentration and a temperature of at least 60°C." *See e.g.* claim 1. Those of skill in the art would recognize that Applicants are in possession of polynucleotide sequences, including sequences containing substitutions, mutations, deletions, that would hybridize to the sequences disclosed in SEQ ID. NO. 2-10 and 12 under the conditions defined in claim 1 and in the specification.

It would be routine for those of skill in the art to use the sequences disclosed to perform genomic analyses. The specification is replete throughout with references for various techniques and specific conditions for performing these analyses, all of which are incorporated by reference. For example, as stated in claim 1 and acknowledged by the Examiner, the specification teaches the stringent hybridization conditions to be used to identify sequences or a complement of SEQ ID No. 2-10 and 12 at page 6, lines 10-21. For example, one of skill in the art would be able to use the disclosed sequences and the disclosed hybridization conditions to identify regions of the 20q13 amplicon that have been amplified via FISH, Southern Blots or quantitative amplification methods (page 27, line 19 - page 29, line 24). One of skill in the art would be able to use Southern Blots or PCR amplification techniques to identify mutant and wild-type forms of specific target genes that hybridize at the defined stringency (*Id.*). The written description requirement does not require identical descriptions of claimed compounds, but it requires enough disclosure in the patent to show one of skill in this art that the inventor 'invented what is claimed.'" *Union oil* 208 F.3d at 1001 quoting *Vas-Cath v. Mahurkar* 935 F.2d 1555, 1563 (Fed. Cir. 1991). The portions of the specification quoted above would convey to one of skill in the art that the Applicants, at the time the application was filed, were in possession of the claimed invention. Applicants respectfully request that the 112, first paragraph rejection be withdrawn.

Obviousness-type double patenting.

Claims 1, 6-13, 23, 45-53, 58-60, and 63 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-9 of U.S. Patent No. 5,892,010 filed July 15, 1996 and issued April 6, 1999. Upon notification of allowable subject matter, Applicants will file a terminal disclaimer, disclaiming any term of any patent granted on the instant application, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. §§154 to 156 and §173, as presently shortened by any terminal disclaimer, of prior Patent No. 5,892,010 issued April 6, 1999, thereby obviating the obviousness-type double patenting rejection.

Claims 1, 6-19, 23 and 45-63 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over non-elected claims 1-21 and 25-29 of copending Application No. 08/785,532, filed January 17, 1997. USSN 08/785,532 was filed as a CPA on November 21, 2000. Upon notification of allowable subject matter in the above referenced application and upon notification of allowable subject matter in USSN 08/785,532, Applicants will file a terminal disclaimer, disclaiming any term of any patent granted on the instant application, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. §§154 to 156 and §173, as presently shortened by any terminal disclaimer, of any patent granted on USSN 08/785,532, thereby obviating the obviousness-type double patenting rejection.

Claims 7, 9, 11, and 13 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claim 8 of U.S. Patent No. 5,892,010 filed July 15, 1996 and issued April 6, 1999. Upon notification of allowable subject matter, Applicants will file a terminal disclaimer, disclaiming any term of any patent granted on the instant application, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. §§154 to 156 and §173, as presently shortened by any terminal disclaimer, of prior Patent No. 5,892,010 issued April 6, 1999, thereby obviating the obviousness-type double patenting rejection.

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Conclusion

In view of the foregoing, Applicants believe all claims are now in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (415) 217-6022.

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on 12/21/00, 2000.

Peter K. Seperack 12/21/00
Attorney for Applicant(s) Date of Signature

Respectfully submitted,

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